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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,976		MARJA TAHTINEN	227-135	6995

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EXAMINER	
SALIMI, ALI REZA	
ART UNIT	**PAPER NUMBER**
1648	10

DATE MAILED: 01/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/622,976	Applicant(s) Tahtinen et al
	Examiner A. R. SALMI	Art Unit 1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 21, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-15* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

This is a response to the amendment B, paper No.9, filed 1/21/2003. Claims 1-15 are pending before the examiner.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, for reasons of record advanced in the previous Office Action mailed 7/18/02. Applicant argues that the term "immunologically active fragment" is defined on page 9, lines 4-5 of the specification. In addition, applicants argue that sequences of (I)-(iii) are from bovine papillomavirus and direct the Office to page 8, lines 11-35 of the specification. Applicant's argument as part of amendment B, Paper NO. 9, filed 1/21/2003 has been considered fully, but they are not persuasive. At the onset applicants are reminded that even though the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, the specification itself does not teach the metes and bounds of the intended regions. Applicants' teaching are general, no boundaries are provided, no sequence is/are given at page 8, lines 11-35. The definition of "immunologically

active fragment" is yet another general term. Applicants are reminded the claims are now drafted towards a "general" bovine papillomavirus expression vector, comprising HIV sequences. Hence, the claims should clearly and distinctly and without any ambiguity recite the boundaries of each and every element that forms the vector. For example, when one looks at the claim and sees the limitation of "Microsomal maintenance element" (MME), and cannot be appraised of its limitations of what is/are the intended metes and bounds of the said element, then the claim is vague and indefinite, since page 8 of the specification does not provide the exact boundaries of the MME that is utilized in the vector. Moreover, with regard to limitation of "immunologically active fragment", since the specification does not set forth the intended metes and bounds of the "fragments" the claim is vague and indefinite. The rejection is maintained.

Claim Rejections - 35 USC § 112

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced in the previous Office Action mailed 7/18/02. Applicants argue that they have shown induction of antibodies in mice and they have monkey data which supports their limitation of vaccine. In addition, applicants argue that since the skill level is high one would know what effective amount to utilize. Moreover, applicants refer to the specification for the teaching of "fragments" capable of eliciting immune response and assert that in the filed of vaccination subunit vaccines are known which consist of immunogenic fragments. Applicant's argument as part of amendment B, Paper NO. 9, filed 1/21/2003 has been considered fully, but they are not

persuasive. Applicants are reminded that as it was stated previously this field is highly unpredictable, and since applicants are the ones who are seeking patent protection they should provide adequate teaching to enable the claimed invention absent any undue experimentation. To date unfortunately no known vaccine for HIV is available. The state of the art recognizes a proper model to be one in which the disease can be replicated in to the model. The HIV disease is not replicable in mice, and mice is not a proper animal model for HIV. One can study the induction of immune response against HIV antigens in mice, but this model does not serve as model for "protective immunity" also referred to as vaccine. The specification has shown induction of immune response in mice, and CTL in monkey, but these where healthy animals. The HIV wasn't replicated in the animals either prior to administration of the claimed vector or after. In addition, for therapeutic vaccine a challenge study should be provided where the disease can be shown to be eradicated. To date no challenge study is present and the state of the art does not recognize the assertions made by the applicants. As it was stated previously there are no challenge study present in the specification to merit the limitation of vaccine against HIV. Induction of immune response is not sufficient showing of protection against a deadly virus a virus-like HIV. A challenge study in an appropriate model where the exact infection or disease can be replicated is needed to show whether or not full protection can be achieved when a full dose of virus is injected. The specification does not show this and undue experimentation would be required to establish such a fact. In addition, applicants dismissal of the evidence cited by the Office is respectfully noted. However, this goes to the heart of the undue experimentation and

state of the art, given the broad limitations of the claimed invention and deficient teaching of the specification at the time of filing. If the post filing evidence shows that in year 2001 the state of the art is contradictory to the broad limitations of the claimed invention, then how is one of ordinary skill in the art is suppose to enable the invention back in 1998? Applicants assertion of having different and opposite post filing experience on vaccine is noted, however, the post filing experience is not part of the record, hence, the Office cannot make an independent judgment of the assertion. Still further, regarding applicants assertion of "sub-unit vaccine", and "fragments" of NEF, REV, and TAT being available. Once again its reiterated that applicants should clearly teach the "sub-unit" vaccine, and since there are no teaching whatsoever in the specification wherein a piece of HIV antigen, i.e Tat, can be inserted in the general bovine papillomavirus vector which shows an induction of immune response or protective response against the HIV fragment, undue experimentation would be required to enable the full scope of the invention. The rejection is respectfully maintained.

In addition, regarding the deposit requirement of plasmids recited in claim 5, applicants assert that they totally disagree with the Office for the deposit. Applicants assert the description of plasmid constructions and the maps set forth in Figures 1 to 4 fully enables the practice of the invention recited in claim 5. Applicants further add, the representation of a plasmid is a manner of choice in both scientific publication and in patent literature, and is fully enabling to those skilled in the art. Applicants conclude the fact that genes of a deathly pathogens are involved does not result in

unusual difficulties in constructing the plasmid carrying such genes. Applicant's argument as part of amendment B, Paper NO. 9, filed 1/21/2003 has been considered fully, but they are not persuasive. At the onset applicants are reminded that this application is a"Utility" type application and not a "Design" application where applicants can obtain patent protection for a plasmid cartoon or "design" of a plasmid. The plasmid of claim 5 are directed to a product. The products which applicants are requesting patent protection for. The figures are cartoons their exact boundaries are not provided and no repeatable method is given so one of skilled in the art can obtain the same product each and every time she/he tries to make the product (emphasis added). The exact boundaries of the various genes involved in making the recited plasmid (products) are not given. There are many steps involved in making the plasmid, all the ligations, digestion, and shuttle vectors utilized do not guarantee that each and every time the same product that is now being claimed would be obtained (emphasis added). Applicants have not provided the exact boundaries of their plasmid so one of ordinary skill in the art would be able to make the exact same product. This is what was argued by the Office which applicants conveniently did not address in their response. If applicants do not appreciate the breadth of their claimed invention the Office certainly does (emphasis added). Applicants specification has provided a general teaching for construction of a vector, but no repeatable method is provided that would give the same plasmid each and every time. Hence, since no such teaching is given the deposit of the plasmid under the terms cited previously would be satisfy of the enablement issue, so one of ordinary skill in the art would have access to the exact structure and would not have to conduct

undue experimentation to enable the claimed invention. In addition, the assertion by the applicants that "the fact that genes of a deathly pathogens are involved does not result in unusual difficulties in constructing the plasmid carrying such genes" is conspired to be an unsupported assertion. Applicants have not provided any evidence to support such assertion. Still further, if applicants conclusion were correct, then no patent claims would incorporate any sequence of any antibody, any vector, or any protein or any vector would be subject to deposit. All applicants would do would be to draw a shape of an antibody on a piece of paper and ask for patent protection, or darw a construct and ask for protection, however, as applicants are well aware such is not the case. The rejection is maintained.

Claim Rejections - 35 USC § 103

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ustav (WO 97/24451), and Hinkula et al (Journal of Virology, July 1997), for reasons of record advanced in the previous Office Action mailed 7/18/02. Applicants argue that Ustav speculates that his vector might also be useful in vaccination and HIV is mentioned together with other pathogenic viruses, and there is no evidence of this effect. Applicants conclude that reasonable expectation is lacking. Applicants add that the reference does not describe any pBN-plasmid that comprise the NEF, REV, or TAT gene as in the present invention. Applicants further add in no way would have been predicated that using such plasmid would result in CTL response which is most effective immune response. With respect to Hinkula reference, applicants argue that they disclosed NEF,

REV, or TAT genes inserted in other kind of vectors. Applicants assert that Hinkula induced immune response against other impurities and not necessarily against NEF, REV, and TAT. Applicants conclude that assuming the combination of references cited by the examiner shows that it would have been obvious to try to prepare vectors resembling the vectors of the present invention by no means one of ordinary skill in the art would have had a reasonable expectation of success. Applicants add, one of ordinary skill in the art would not have reasonably expected that the use of pBN vectors would result in highly specific antibody response and a CTL response capable of destroying HIV infected cells early in viral infection cycle as disclosed in the present application. Applicant's argument as part of amendment B, Paper NO. 9, filed 1/21/2003 has been considered fully, but they are not persuasive. First, Applicants' assertion of pBN vectors inducing CTL response capable of destroying HIV infected cells early is viral specific infection cycle is considered erroneous and has no support what-so-ever. This application has not provided any evidence that shows the pBN plasmid are able to destroy HIV infection whether the infection is early or late (emphasis added). Inducing immune response in healthy animals is not equivalent of destroying HIV, and it would not have been unexpected given the teaching of the cited prior art, Hinkula et al also taught T cell proliferation (see Table 3). The result of animal study in the specification which applicants refer to as "unexpected" is noted, but the animals where never infected with HIV, applicants have shown induction of immune response in healthy animals absent any HIV infection. Still further, contrary to applicants assertion, this is a situation of obvious to try and obvious to succeed (emphasis added). Given the ample teaching provided in the above

cited art and the level of skill in the art as applicants are on record and admit that the level is rather high in this art and the sequences of NEF, REV, and TAT are all available in public, this is a situation of obvious to try and obvious to succeed. Still further, applicants remark regarding the teaching of Hinkula et al is unsupported. There are no head to head study presented to refute the said teaching, especially given the CTL data of Table 3 taught by Hinkula et al is as impressive as applicants. The above cited art collectively teach the claimed invention. The cited art provided the vector, Ustav et al, including pBN (see Figure 7 A-C) and all that is involved in making the vector and further taught that it can be utilized in expression of all types of pathogens including HIV. In addition, Hinkula et al taught plasmid immunization of NEF, REV, and TAT. Given the level of skill in the art and the familiarity of one skill in the art with the above cited art the Office maintains one of skill in the art would have been highly motivated to insert the NEF, REV, and TAT as taught by Hinkula et al into the vector taught by Ustav et al to induce immune response against HIV absent any unexpected results. Induction of CTL in mice, or monkey where no HIV was present is not considered to be unexpected. The rejection is respectfully maintained.

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woo et al (WO 94/12629), and Hinkula et al (Journal of Virology, July 1997), for reasons of record advanced in the previous Office Action mailed 7/18/02. Applicants argue that Hinkula et al disclosed NEF, REV, or TAT genes inserted in other kind of vectors. Applicants assert that Hinkula et al induced immune response against other impurities and not necessarily against NEF,

REV, and TAT. In addition, applicants add that the deficience of are not remedies by Woo et al which generally disclosed a general self replicating vectors without the specific HIV genes. Applicants argue that even the knowledge of vectors disclosed by Woo et al and the results of Hinkula et al would not have motivated one skilled in the art, due to the complexity of the vectors, to construct vectors of present invention, let alone with a reasonable expectation of success. Applicant's argument as part of amendment B, Paper NO. 9, filed 1/21/2003 has been considered fully, but they are not persuasive. First, applicants make rather interesting comment asserting that the vectors are "complex", and yet, when complexity issue is raised by the Office applicants dismiss the rejection raised by the Office as routine and everything being known in the public domain. Please reconcile. What complexity is involved for inserting a known sequence into a known vector to induce immune response? In addition, why wouldn't one expect success? Complexity lies in induction of immune response against immun.-compromised host infected with HIV, which applicants have not provided any guidance. Hinkula et al observed success. Hinkula et al taught DNA immunization of plasmid wherein each plasmid comprised TAT, NEF, or REV or HIV (see the abstract, and Table 3). In addition, they clearly taught that plasmid DNA carrying any of three HIV genes of NEF, REV, TAT induced immune response in mice (see bridging paragraph of page 5535-5536). Woo et al (WO 94/12629) taught the self-replicating vector comprising E1, E2 genes, minimal origin of replication of papillomavirus (MO), a papillomavirus microchormosomal maintenance element (MME) being able to express heterologous genes. This is an obviousness rejection and not an anticipation rejection. Given the

ample teaching taught by the above cited art one of skill in the art would have been motivated to place the TAT, NEF, and REV as they are well known in the art and publicly available, and further taught by Hinkula et al into the general vector taught by Woo et al to induce immune response, absent unexpected results. The rejection is maintained.

NEW GROUNDS OF REJECTION:

Claim Rejections - 35 USC § 112

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite for recitation of "and a nucleotide sequence encoding a fragment thereof", what does this mean? The sequence is not defined, and the fragments are not defined. In addition, the intended nucleotide sequence of NEF, REV, and TAT are not defined.

Claim 7 is vague and indefinite for recitation of "A vaccine for DNA immunization against HIV", what does this mean? Is the intent to immunize a DNA? Is "A DNA Vaccine against HIV" intended? In addition, the claim is confusing for recitation of "a mixture of vectors", what are these vectors? Is a baculovirus and poxvirus mixture intended?

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: when to administer the vaccine, the effective amount, and how the induction of CTL is induced, etc.. In addition, is the person immunocompetent or immun.-compromised person intended?

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: when to administer the vaccine, the effective amount, and how the induction of CTL is induced, etc.. In addition, is the person immunocompetent or immun.-compromised person intended?

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the effective amount, etc.. In addition, is the person immunocompetent or immun.-compromised person intended?

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the effective amount, the mixture of vectors, etc.. In addition, is the person immunocompetent or immun.-compromised person intended? The intended mixture vectors are not defined. Is the mixture of vaccinia and baculovirus intended?

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to A. R. Salimi whose telephone number is (703) 305-7136. The examiner can normally be reached on Monday-Friday from 9:00 Am to 6:00 Pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is (703) 305-3014, or (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

A. R. Salimi

1/30/2003

ALI R. SALIMI
PRIMARY EXAMINER